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Title

Commentary in response to the letter from Farsalinos et al. regarding our publication entitled: "Identification of toxicants in cinnamon-flavored electronic cigarette refill fluids"

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Letter to the Editor

Cytotoxicity of cinnamon-flavored electronic cigarette refills: Are the results truly applicable to electronic cigarette use?



We read with particular interest the study by Behar et al. (2013) evaluating the cytotoxic potential of cinnamon-flavored liquids used for electronic cigarettes (ECs). The authors concluded that determining the cytotoxicity of a specific flavoring will be an integral part of improving EC safety. Although this is principally correct, in reality they did not evaluate EC use and did not examine any sample in the way used by EC consumers. Instead, they tested the samples in their original liquid form. Such methodology does not deliver the EC liquid in the designated manner and is less relevant than vapor generation of the liquid via activation of the electronic device (Romagna et al., 2013). It is possible that not all liquid constituents evaporate at the same manner or in similar concentrations. In the case of cinnamon flavoring, cinnamaldehyde has an evaporation temperature of 246 °C compared to a temperature of 138 °C for a 10% water–90% glycerol mixture typically used in EC liquids (Flick, 1998). Due to this, concentration of cinnamaldehyde may be lower in vapor compared to liquid. Therefore, it is unlikely that such testing could provide insights about the vapor effects. A recent study by our group found that vapor produced by a cinnamon-flavored refill liquid was marginally cytotoxic on cultured cardiomyoblasts, however cytotoxicity was lower compared to cigarette smoke by orders of magnitude (Farsalinos et al., 2013).

An interesting finding of the study by Behar et al. was that cinnamaldehyde levels differed by up to 100 times between samples. This raises the possibility that some of the samples tested were concentrated flavors, which are used only after being diluted. In fact, after searching on internet shops and communicating with manufacturers we were able to detect at least 4 samples (#22: Cinnamon Ceylon; #53 and #69: Sinful Cinnamon Tasty Puff; #61: Cinna-bun) which are exclusively available in concentrated forms that need to be diluted in a mixture of glycerol, propylene glycol and nicotine before being used with ECs. Therefore, even if vapor was produced using these samples, the results would not represent realistic EC use because they are not ready-to-use liquids. It seems that the authors were either un- or mis-informed about the availability of a huge variety of flavorings in concentrated form (used for what is known as “do it yourself” liquid preparation) and this may be the reason for mistakenly characterizing these samples as refill liquids.

Cinnamaldehyde is Generally Recognized As Safe (GRAS) by the Flavoring Extract Manufacturers' Association, is approved for food use (21 CFR 182.60) by the Food and Drug Administration and is used in the food industry at levels up to 4900 ppm (which

corresponds to approximately 4×10^{-2} M – EPA, 2010). The safety of cinnamaldehyde intake has been evaluated at currently recommended doses by cytotoxicity studies in experimental animals (NTP, 2004); however, Behar et al. found cinnamaldehyde to be cytotoxic at a significantly lower dose and this should raise concern about the effects of cinnamaldehyde intake, rather than inhalation, in sensitive cell lines such as human embryonic stem cells.

In conclusion, we believe that the methodology and sample selection are major limitations of this study and raise doubts about the applicability of the results to EC use. Testing the samples in liquid form would be more relevant to usage as a food additive rather than as an EC liquid, especially for those samples which were concentrated flavors rather than refills. It is important to define the safety levels of cinnamaldehyde (and every flavor) used in ECs; however, this should be determined by examining the effects of vapor rather than liquid.

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Conflicts of interest

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